JACC Vol. 15, No. 4
March 15, 1990:814–5

Editorial Comment

Impaired Left Ventricular Relaxation in Hypertrophic Cardiomyopathy: Relation to Extent of Hypertrophy*

E. DOUGLAS WIGLE, MD

Toronto, Ontario, Canada

Background. Impaired diastolic filling of the left (1,2) or right ventricle, or both, in hypertrophic cardiomyopathy has been recognized for almost 30 years. Although the obstruction to left ventricular outflow was the focus of attention in hypertrophic cardiomyopathy in the 1960s, it was recognized that some patients could be more disabled from abnormal diastolic filling than from the outflow obstruction in systole (2). In the 1960s the resulting ventricular end-diastolic pressure elevations were attributed to decreased ventricular compliance (dv/dp), which today would be described as increased chamber stiffness (dp/dv). Ventricular relaxation was not discussed because it was not well understood and there were limited means to measure it.

This state of affairs has changed drastically in the past 20 years as the result of two developments. First, our understanding of the three factors controlling ventricular relaxation (load, deactivation and nonuniformity) has improved dramatically as the result of the basic research of Brutsaert and others (3,4). Second, modern cardiologic technology has made available to us numerous methods by which ventricular relaxation can be quantitatively assessed (5). These developments have resulted in the appreciation that impaired ventricular relaxation is usually, but not always, more important than increased chamber stiffness in explaining abnormal diastolic filling in hypertrophic cardiomyopathy (5).

The present study. In this issue of the Journal, Spirito and Maron (6) report that impaired left ventricular relaxation in hypertrophic cardiomyopathy, determined by means of Doppler mitral inflow velocities, is not related to the extent of left ventricular hypertrophy, determined by cross-sectional two-dimensional echocardiographic views of the left ventricle. In a previous study (7) using M-mode echocardiographic techniques to document impaired relaxation, these authors found a relation between the extent of hypertrophy and impaired left ventricular relaxation. In both studies they report significant relaxation impairment with only mild degrees of hypertrophy (6,7). The present study is very dependent on how well Doppler mitral inflow velocities reflect left ventricular relaxation and how well cross-sectional echocardiographic views of the left ventricle reflect the true extent of hypertrophy in hypertrophic cardiomyopathy.

Normally, left ventricular relaxation is primarily load dependent, although if deactivation is grossly depressed, relaxation may become load independent (3,4). Thus, in the absence of mitral stenosis, the major determinant of peak early mitral inflow velocity is the left atrial–left ventricular pressure difference in early diastole (8). In addition to left ventricular relaxation this pressure difference is influenced by left atrial pressure at the time of mitral valve opening, the passive viscoelastic properties of the left ventricle and a number of other factors (8). Low left atrial pressure may result in mitral inflow velocities that suggest impaired relaxation (for example, a low early and late diastolic peak flow velocity [E/A] ratio), whereas high left atrial pressure (particularly with a high *v* wave) may normalize the mitral inflow velocity (for a normal or high E/A ratio) that would otherwise reflect impaired relaxation if the left atrial pressure had not been elevated (8). The authors have tried to correct for these possibilities, but total correction is not possible without knowing the left atrial pressure in all patients.

In the present study, the extent of left ventricular hypertrophy has been estimated by a cross-sectional view of the left ventricle at the level of the mitral leaflet tips or papillary muscles (6). We (5) have described a 10 point scoring system to evaluate the extent of left ventricular hypertrophy in hypertrophic cardiomyopathy that takes into account septal thickness and extent of septal hypertrophy from base to apex, as well as anterolateral wall involvement. This scoring system correlates well with left ventricular mass determined by nuclear magnetic resonance imaging (9). Using this system, Utsunomiya and associates (10) found that both M-mode and Doppler echocardiographic indexes of impaired relaxation correlated with the extent of hypertrophy. Similarly, we found that some, but not all, nuclear angiographic indexes of impaired relaxation (9,11), as well as the degree of left ventricular end-diastolic pressure elevation (5), correlated with the extent of hypertrophy.

It must be appreciated that ventricular relaxation is an extremely complex phenomenon that may be influenced by no fewer than five hemodynamic loads, as well as by the process of deactivation and the degree of nonuniformity of

*Editorials published in *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of JACC or The American College of Cardiology.

From the Division of Cardiology, Department of Medicine, Toronto General Hospital, University of Toronto, Toronto, Ontario, Canada.

Address for reprints: E. Douglas Wigle, MD, 12-217 Eaton North, Toronto General Hospital, 200 Elizabeth Street, Toronto, Ontario, Canada M5G 2C4.

0735-1097/90/$3.50

load and deactivation in space and time (3–5). There are many indexes of relaxation measured by a number of different techniques, and although there may be correlations among some of these indexes (12), they should not necessarily be equated with one another (8). There are reasons to think that left ventricular relaxation in hypertrophic cardiomyopathy is related to the extent of hypertrophy (5), but if internal or external restoring forces, or both, are excessive (5) or if left atrial pressure is markedly elevated in cases of extensive hypertrophy, indexes that reflect left ventricular relaxation could be normalized (5,8). Conversely, if left atrial pressure is significantly lower in cases of mild hypertrophy, indexes of left ventricular relaxation could be abnormal as a result of the load dependence of relaxation (3,4,8).

Clinical implications. It is important today for clinicians to appreciate that impaired ventricular relaxation usually results in reduced rapid ventricular filling and, in compensation, exaggerated atrial systolic filling (5,13,14) unless significant left atrial pressure elevation normalizes the pattern of filling (8). Conversely, increased passive chamber stiffness (decreased compliance) results in a restrictive pattern of ventricular filling in which there is exaggerated rapid early filling and normal or reduced atrial systolic filling. Although it has been repeatedly reported that a fourth heart sound reflects a stiff or noncompliant ventricle, our observations of patients with hypertrophic cardiomyopathy (14) strongly suggest that a fourth heart sound reflects impaired left ventricular relaxation and results from the exaggerated atrial systolic filling under these circumstances. Similarly, we have noted a loud third heart sound in patients with restriction of ventricular filling that is believed to be due to rapid ventricular filling in early diastole. These observations are in keeping with the assumption that third and fourth heart sounds are ventricular distension sounds (14).

A corollary to these observations is the fact that patients with marked impairment of relaxation accompanied by a loud fourth heart sound suffer dire hemodynamic consequences with the onset of atrial fibrillation, principally because of a loss of atrial systole, the most important compensatory mechanism for impaired relaxation (5,13,14). Conversely, patients with a loud third heart sound (caused by restriction or constriction of ventricular filling) may not deteriorate significantly with the onset of atrial fibrillation because atrial systole contributes little to ventricular filling under these circumstances (5,14).

Conclusions. Impairment of active ventricular relaxation is an extremely important concept in clinical cardiology today and must be distinguished from increased passive chamber stiffness (decreased compliance). Impaired ventricular relaxation is often a more important cause of abnormal diastolic filling than is increased chamber stiffness, but both abnormalities may coexist in patients with ventricular hypertrophy, coronary artery disease and a number of other cardiac conditions.

References

1. Braunwald E, Morrow AG, Cornell WP, Aygen MM, Hilbish TF. Idiopathic hypertrophic subaortic stenosis. Am J Med 1960;29:924–45.

2. Wigle ED, Heimbecker RO, Gunton RW. Idiopathic ventricular septal hypertrophy causing muscular subaortic stenosis. Circulation 1962;26: 325–40.

3. Brutsaert DL, Housmans PR, Goethals MA. Dual control of relaxation. Its role in the ventricular function in the mammalian heart. Circ Res 1980;47:637–52.

4. Brutsaert DL, Rademakers FE, Sys SU. Triple control of relaxation: implications in cardiac disease. Circulation 1984;69:190–6.

5. Wigle ED, Sasson Z, Henderson MA, et al. Hypertrophic cardiomyopathy: the importance of the site and extent of hypertrophy. A review. Prog Cardiovasc Dis 1985;28:1–83.

6. Spirito P, Maron BJ. Relation between extent of left ventricular hypertrophy and diastolic filling abnormalities in hypertrophic cardiomyopathy. J Am Coll Cardiol 1990;15:808–13.

7. Spirito P, Maron BJ, Chiarella F, et al. Diastolic abnormalities in patients with hypertrophic cardiomyopathy: relation to magnitude of left ventricular hypertrophy. Circulation 1985;72:310–16.

8. Appleton CP, Hatle LK, Popp RL. Relation to transmitral flow velocity patterns to left ventricular diastolic function: new insights from a combined hemodynamic and Doppler echocardiographic study. J Am Coll Cardiol 1988;12:426–40.

9. Liu P, Wilansky S, Poon P, et al. Myocardial mass quantitation by magnetic resonance imaging in hypertrophic cardiomyopathy (abstr). Circulation 1986;74(suppl II):II-226.

10. Utsunomiya T, Gardin JM, Henry WL. Relationship between the extent of muscular hypertrophy and diastolic function in patients with hypertrophic cardiomyopathy without left ventricular outflow gradients or mitral regurgitation (abstr). J Am Coll Cardiol 1989;13(suppl. A):89A.

11. Sasson Z, Lefkowitz CA, Langer G, et al. Diastolic dysfunction in hypertrophic cardiomyopathy. Importance of the extent of hypertrophy (abstr). Clin Invest Med 1985;8:60.

12. Spirito P, Maron BJ, Bonow RO. Noninvasive assessment of left ventricular diastolic function: comparative analysis of Doppler echocardiographic and radionuclide angiographic techniques. J Am Coll Cardiol 1986;7:518–26.

13. Bonow RO, Frederick TM, Bacharach SL, et al. Atrial systole and left ventricular filling in hypertrophic cardiomyopathy: effect of verapamil. Am J Cardiol 1983;51:1386–91.

14. Wigle ED. Hypertrophic cardiomyopathy: a 1987 viewpoint. Circulation 1987;75:311–22.